Libyan international Medical University

Faculty of Basic Medical Science

Homocysteine as a Risk Factor for Atherosclerosis

Submitted by : Mohamed Younes Mohamed**(**1546**)**, Second Year Medical Student.

Supervisor : Sara El Mgerhy

Date of Submission : 5 / 5 / 2018

This Report Was submitted to fulfill the requirements for the 2y Medical Student

Abstract:
This study aimed to review the role of homocysteine as a risk factor in the pathogenesis of atherosclerosis and atheroma, and to provide recommendations for the treatment of hyperhomocysteinemia.

Introduction:
Homocysteine is a sulphurated amino acid which, at high plasma concentrations, predisposes to thrombosis and induces focal arteriosclerosis. These characteristics have been established both in patients with homocystinuria, a genetic disease in which homocysteine accumulates in the blood.[1]In addition it must be emphasized that the vascular disease in homocystinuria due to cystathionine β-synthase (CBS) deficiency, methylenetetrahydrofolatereductase (MTHFR) deficiency, or inborn errors in cobalamin metabolism bears little resemblance to the atherosclerotic and atherothrombotic vascular disease seen in the adult general population. Atherosclerosis is characterized by a thickening of the arterial wall due to smooth muscle cell proliferation, lipid deposits, and fibrosis.[2]Rupture of the lipid-containing atherosclerotic plaques results in thrombosis (atherothrombosis) and leads to myocardial infarction and stroke.The first indication that sulfur amino acid metabolism is linked to atherosclerosis came from observations in 1953 demonstrating that pathogenic cholesterol concentrations and experimental atherogenesis in monkeys can be inhibited by dietary methionine[3]. Since the early 60s elevated homocysteine levels in blood (hyperhomocysteinemia) caused by different deficiencies of sulfur amino acid metabolism were reported to be associated with vascular disease and, in particular, with atherosclerotic plaque formation. Today, Hcy is recognized by many studies as a strong, independent and causal risk factor for atherosclerosis.[4,5]

Discussion:
My report result based on 2 studies :
The 1st study which said :
There is appositive correlation has been demonstrated between homocysteine concentrations and coronary atherosclerosis.[6] aprospective study[7] of 587 patients with angiographically confirmed coronary artery disease followed for five years found a strong, graded relationship between elevated homocysteine and mortality. After age and gender, the strongest predictors of mortality were total homocysteine concentrations, ejection fraction, and serum creatinine. Using total homocysteine concentrations <9 μmol/L as the reference point, researchers adjusted for age and gender yet still found the mortality ratio to increase as the homocysteine concentration increased. The mortality ratio was 3.3, 6.3, and 9.9 for patients with homocysteine concentrations of 9. 0 – 14.9, 15.0 – 19.9, and ≥20.0 μmol/L, respectively.
The 2nd study:
he presence of mild to moderate hyperhomocysteinemia is an independent risk factor for atherosclerosis in the coronary, cerebral, and peripheral vasculature, and for vascular disease, including coronary disease. It has been demonstrated that plasma total homocysteine level is a strong predictor of mortality in patients with angiographically confirmed coronary artery disease. Hvpothesis: The study was undertaken to determine the extent of homocysteine levels in patients without documented coronary artery disease, but with at least one risk factor for atherosclerosis. Methods: Fasting blood samples were collected prospectively from 160 consecutive patients (50 women and 110 men, mean age from 7 to 65 years) who had at least one risk factor for atherosclerosis, but had no documented coronary artery disease. Homocysteine levels were measured by an immunoassay method. Resulrs: Of the patients studied, 78 (48.75%) with at least one risk factor for atherosclerosis had high homocysteine levels; 62 patients had mild hyperhomocysteinemia (15-30 pmol/l); and 16 patients had moderate hyperhomocysteinemia. However, the all studies show the same conclusion.[8]
The treatment:
Although no long-term clinical trials have assessed the risk of atherosclerosis when patients with elevated homocysteine concentrations are treated, early studies indicate that treatment may be beneficial in reducing homocysteine concentrations. Although the long-term benefits of treating elevated homocysteine concentrations (such as prevention of atherosclerosis) are not known, treatment currently accepted in those patients with high homocysteine concentrations is folic acid use either alone or in combination with certain B vitamins.6 The optimal dose of folic acid has yet to be determined; however, doses ranging from 650 μg to 10 mg per day have been shown to be effi cacious. Treatment should continue for the patient's lifetime, as homocysteine concentrations return to baseline within ten weeks of discontinuing treatment. In addition to treatment with B vitamin supplementation, patients must carefully monitor their diet and limit the intake of foods and beverages (coffee) that raise homocysteine concentrations and increase the risk of atherosclerosis.

Patients should be encouraged to increase their intake of folic acid and vitamins B6 and B12 , as contained in fortified cereals, leafy green vegetables, fruits, beef, poultry, and fish.6 Fi n a l l y , more prospective, long-term trials are needed in patients with atherosclerosis to define the benefits of treatment on morbidity and mortality.[9]

Conclusion:

Retrospective and prospective studies demonstrate a positive correlation between high homocysteine concentrations and atherosclerosis. Most recently, a study has shown an increase in mortality in patients with elevated homocysteine concentrations compared with healthy volunteers , in addition The treatment of choice for hyperhomocysteinemia is folic acid.

References:

1.https://www.ncbi.nlm.nih.gov/pubmed/9137733.

2. Davies MJ.Stability and instability: two faces of coronary atherosclerosis. The Paul Dudley White Lecture 1995. Circulation 1996; 94:2013–20.

3. G. V. Mann, S. B. Andrus, N. A. Mc, and F. J. Stare, "Experimental atherosclerosis in Cebus monkeys," Journal of Experimental Medicine, vol. 98, pp. 195–218, 1953.

4. J. Zhou, G. H. Werstuck, S. Lhotak et al., "Hyperhomocysteinemia induced by methionine supplementation does not independently cause atherosclerosis in C57BL/6J mice," Journal of the Federation of American Societies for Experimental Biology, vol. 22, no. 7, pp. 2569–2578, 2008.

5. K. S. McCully, "Homocysteine, vitamins, and vascular disease prevention," American Journal of Clinical Nutrition, vol. 86, no. 5, pp. 1563S–1568S, 2007.

6. Schwartz SM, Siscovick DS, Malinow R, Rosendaal FR, Beverly K, Hess DL, et al. Myocardial infarction in young women in relation to plasma total homocysteine, folate, and a common variant in the methylenetetrahydrofolate reductase gene. Circulation 1997;96:412-7.

7. Nygard O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine concentrations and mortality in patients with coronary artery disease. N Engl J Med 1997;337:230-6.

8. Stampfer MJ, Malinow MR, Willet WC, Newcomer LM, Upson B, Ullman D, Tishler PV, Hennekens CH: A prospective study ofplas- ma homocysteine and risk of myocardial infarction in US physi- cians. JAm MedAssoc 1992;268:887-88.

9. Malinow MR, Bostom AG, Krauss RM. Homocysteine, diet, and cardiovascular diseases. A healthcare statement for healthcare professionals from the nutrition committee. American Heart Association. Circulation 19 9 9 ; 9 9 : 1 7 8 - 8 2 .